PATENT COOPERATION TREATY

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COPY

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PRO025/4-012	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US04/18731	International filing date (*day/month/year*) 08 June 2004 (08.06.2004)	(Earliest) Priority Date (*day/month/year*) 09 June 2003 (09.06.2003)
Applicant BAYLOR COLLEGE OF MEDICINE		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**
   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      ☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. ☐ **Certain claims were found unsearchable** (See Box No. II)
3. ☒ **Unity of invention is lacking** (See Box No. III)
4. With regard to the **title**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,
   a. the figure of the **drawings** to be published with the abstract is Figure No. ____
      ☐ as suggested by the applicant.
      ☐ as selected by this Authority, because the applicant failed to suggest a figure.
      ☐ as selected by this Authority, because this figure better characterizes the invention.
   b. ☒ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/18731

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1,2 and 6-8

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/18731

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12Q 1/68; C07H 21/04
US CL : 435/6; 536/23.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6; 536/23.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RICH et al. RTVP-1, a novel human gene with sequence similarity to genes of diverse species, is expressed in tumor cell lines of glial but not neuronal origin. Gene. 1996, Vol. 180, pages 125-130, especially page 126, 1st column, 1st paragraph; page 129, 2nd column, 2nd paragraph.	1, 2, and 6-8

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
19 July 2005 (19.07.2005)

Date of mailing of the international search report
28 JUL 2005

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Authorized officer
Young J. Kim
Telephone No. (571) 272-1600

Form PCT/ISA/210 (second sheet) (January 2004)

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1, 2, and 6-8, drawn to an isolated nucleic acid pertaining to SEQ ID NO: 2, a vector comprising said isolated nucleic acid, and a host cell comprising said vector, and a method of its use to express a polypeptide.

Group II, claim(s) 3 and 9-12, drawn to an isolated polypeptide pertaining to SEQ ID NO: 2 and a kit comprising the polypeptide.

Group III, claim(s) 4 and 5, drawn to an antibody, monoclonal for detecting polypeptide pertaining to SEQ ID NO: 2.

Group IV, claim(s) 13, drawn to RGL receptor protein that binds polypeptide of SEQ ID NO: 2.

Group V, claim(s) 14, 15, and 19-21, drawn to an isolated nucleic acid pertaining to SEQ ID NO: 3, a vector comprising said nucleic acid, a host cell comprising said vector, and a method of the use of host cell.

Group VI, claim(s) 16, 22-25, 27-31, and 38, drawn to an isolated protein of SEQ ID NO: 4, a kit comprising said protein, and a vaccine comprising said protein.

Group VII, claim(s) 17, 18, and 32-37, drawn to an antibody, monoclonal antibody directed to polypeptide of SEQ ID NO: 4, a kit comprising said antibody, and a hybridoma producing said antibody.

Group VIII, claim(s) 26, drawn to RGL receptor that binds the protein of SEQ ID NO: 4.

Group IX, claim(s) 39-43, drawn to a method of treating a patient via administration of the polypeptide of SEQ ID NO: 4.

Group X, claim(s) 44-48, drawn to a method of treating a patient via administration of the polypeptide of SEQ ID NO: 2.

Group XI, claims 49-52, drawn to a composition comprising a vector comprising the promoter for RGL to any gene.

Group XII, claim(s) 53-57, drawn to a method of treating a patient via administration of the nucleic acid of SEQ ID NO: 1.

Group XIII, claim(s) 58-62, drawn to a method of treating a patient via administration of the nucleic acid of SEQ ID NO: 3.

The inventions listed as Groups I-XIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups I-IV lack unity of invention based on that the nucleic acids, polypeptides, antibodies, and receptor proteins are all structurally unrelated, the conditions of which govern their use are also unrelated.

Groups V-VIII lack unity of invention based on that the nucleic acids, polypeptides, antibodies, and receptor proteins are all structurally unrelated, the condition of which govern their use are also unrelated.

Further, Groups I-IV lack unity of invention from Groups V-VIII because Groups I-IV pertain to a nucleic acid of SEQ ID NO: 1 and its encoded protein of SEQ ID NO: 2, while Groups V-VIII pertain to a different isoform of the nucleic acid of SEQ ID NO: 3 and its encoded protein of SEQ ID NO: 4, structurally unrelated in that they comprises different sequences.

Groups IX and XIII lack unity of invention from Group I-IV because Groups IX and XIII pertain to the protein of SEQ ID NO: 4 and the nucleic acid of SEQ ID NO: 3, while Groups I-IV pertain to the protein of SEQ ID NO: 2 and the nucleic acid of SEQ ID NO: 1, disclosed as being different in sequences, thus unrelated in structure, lacking in the unity of invention.

Group X and XII lack unity of invention from Groups V-VIII because Groups X and XII pertain to the protein of SEQ ID NO: 2 and the nucleic acid of SEQ ID NO: 1, while Groups V-VIII pertain to the protein of SEQ ID NO: 4 and the nucleic acid of SEQ ID NO: 3, disclosed as being different in sequences, thus unrelated in structure, lacking in the unity of invention.

Group XI lacks unity of invention from Groups I-X, XII, and XIII because the composition of Group IX has no relation to the nucleic acid or polypeptide of SEQ ID Numbers 1 and 2; and SEQ ID Numbers 3 and 4, respectively.

Additionally, with regard to Groups IX, X, XII, and XIII, 37 CFR 1.475 (b), states that claims drawn to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combination of categories:

(1) A product and a process of producing the product
(2) A product and a process of using the product
(3) A product, process of producing the product, and a process of using the product
(4) A process and an apparatus or means to carryout the process
(5) A product, a process of producing the product, and an apparatus of means to carryout the process.

An application containing claims to more or less than one of the "combinations of categories" of inventions set forth above, unity of invention might not be present. (MPEP 1850).

Inventions covered by Groups I, II, V, and VI comprise a product, a method of producing the product, and/or method of using the product as required in 37 CFR 1.475 (b). Because the Groups already include one of the above combinations, any additional categories of inventions in Groups IX, X, XII, and XIII have been determined to lack unity of invention in pursuant to 37 CFR 1.475(b).

Continuation of B. FIELDS SEARCHED Item 3:
Patent Databases
NPL (Eslevier)
search terms: RGL, RTVP-1.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
DAVID K. WOOTEN
VINSON & ELKINS L.L.P.
2300 FIRST CITY TOWER
1001 FANNIN STREET
HOUSTON, TX 77002-6760

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	28 JUL 2005
Applicant's or agent's file reference PRO025/4-012	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US04/18731	08 June 2004 (08.06.2004)	09 June 2003 (09.06.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C12Q 1/68; C07H 21/04 and US Cl.: 435/6; 536/23.1

Applicant

BAYLOR COLLEGE OF MEDICINE

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☒ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Young J. Kim Telephone No. (571) 272-1600

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/18731

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/18731

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
   - ☐ paid additional fees
   - ☐ paid additional fees under protest
   - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
   - ☐ complied with
   - ☒ not complied with for the following reasons:

   See the lack of unity section of the International Search Report(Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:
   - ☐ all parts.
   - ☒ the parts relating to claims Nos. 1,2 and 6-8

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/18731

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 7 and 8	YES
	Claims 1, 2, and 6	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1, 2, and 6-8	NO
Industrial applicability (IA)	Claims NONE	YES
	Claims 1, 2, and 6-8	NO

2. Citations and explanations:

Please See Continuation Sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/18731

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Please See Continuation Sheet

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:
Claims 1, 2, and 6 lack novelty under PCT Article 33(2) as being anticipated by Rich et al. (Gene, 1996, vol. 180, pages 125-130).

Rich et al. disclose RTVP-1 nucleic acid (Figure 1).
According to the instant description RTVP-1 shows significant homology to that of RGL-alpha (or SEQ ID NO: 1), which, based on homology, would necessarily hybridize under the recited moderately stringent conditions. Additionally, as RTVP-1 sequence could be produced by the mutagenesis of SEQ ID NO: 1, the nucleic acid of Rich et al. would also anticipate the nucleic acid of the embodiment d).
With regard to claims 2 and 6, Rich et al. discloses that their nucleic acid was subcloned (page 126, 1st column, 1st paragraph) demonstrating the vector comprising the nucleic acid and a host cell comprising said vector.

Therefore, Rich et al. anticipate the invention as claimed.

Claims 7 and 8 lack an inventive step under PCT Article 33(3) as being obvious over Rich et al. (Gene, 1996, vol. 180, pages 125-130).

Rich et al. disclose RTVP-1 nucleic acid (Figure 1).
According to the instant description RTVP-1 shows significant homology to that of RGL-alpha (or SEQ ID NO: 1), which, based on homology, would necessarily hybridize under the recited moderately stringent conditions. Additionally, as RTVP-1 sequence could be produced by the mutagenesis of SEQ ID NO: 1, the nucleic acid of Rich et al. would also anticipate the nucleic acid of the embodiment d).
Rich et al. discloses that their nucleic acid was subcloned (page 126, 1st column, 1st paragraph) demonstrating the vector comprising the nucleic acid and a host cell comprising said vector.

Rich et al. do not produce the polypeptide encoded by their nucleic acid.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to express the protein encoded by the nucleic acid of Rich et al,. given the explicit motivation provided by the artisans:
"Further work will be required to determine whether the expression of RTVP-1 transcripts in tumor cell lines is related to their malignant characteristics....RTVP-1 may participate in a response to cellular damage or may play a role in tissue remodeling and cell death..." (page 129, 2nd column, 2nd paragraph).
Hence, one of ordinary skill in the art at the time the invention was made would have been motivated to employ the nucleic acid of Rich et al. so as to produce a polypeptide, in order to determine whether the expression of RTVP-1 transcripts would play a role in tissue remodeling and cell death, with a reasonable expectation of success.

Therefore, the invention as claimed is obvious over the cited reference.

Claims 1, 2, and 6-8 lack industrial applicability as defined by PCT Article 33(4).

The instant description states that a cDNA was identified using homology search and PCR-based approaches that correspond to a

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

reported sequence, RTVP-1/CliPR-Like (RGL) in the NCBI database and that RT-PCR analysis indicates that this sequence and an unknown cDNA is identical to RGL except for a 27 base pair/9 amino acid insertion. While the instant description generically states that "a cDNA" was identified, the instant description does not indicate whether this cDNA is the nucleic acid of SEQ ID NO: 1. Further, even if this cDNA was the nucleic acid of SEQ ID NO: 1, the entire basis for the asserted use is based on its homology to a known RGL sequence, MGC26856. Homology based assertion of a nucleic acid, absent empirical validation, lacks industrial applicability because a single shift in the reading frame would encode an entirely different protein. In addition, the claimed nucleic acid contains mismatches which occur along the length of the known RTVP-1 nucleic acid (Figure 1). It is well-established that even a single amino acid substitution would perturb a protein's function. The instant description neither discloses where the insertion occurs nor that the claimed nucleic acid is empirically validated as an RGL polypeptide. While the description states that Figure 3 shows various potential p53 binding sites within the % identity to a p53 consensus sequence, the description does not give any evidence that the p53, in fact, binds to the claimed nucleic acid of SEQ ID NO: 1.
While example 3 on page 41 of the description purports that TRE-cDNA construct is stably transfected to CMV-rtTA TSUPr1 human prostate cancer and that Figure 5 demonstrates the comparison of the ability of RGL-alpha, RGL-beta, RTVP-1 and p53 to induce apoptosis, the description is ambiguous as to whether the claimed nucleic acid of SEQ ID NO: 1 is involved in the examples.

Claims lack industrial applicability therefore.

VIII. The following observations on the clarity of the claims, description, and drawings or on the questions, are made:
Claims 1, 2, and 6-8 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims are indefinite for the following reason(s):

Claim 1 is indefinite because the claim recites that the nucleic acid is selected from the group consisting of, but the actual members of the groups are related by "or," rather than, "and." Therefore, it becomes confusing what that actual group is wherein the nucleic acid is selected "from."

Claims 2 and 6-8 are indefinite by way of their dependency on claim 1.

Claim 1 is indefinite for the following reasons:
Claim 1 recites that the nucleic acid is selected from a group, wherein the group contains the below two members:
b) an isolated nucleic acid molecule encoding the amino acid sequence comprising SEQ ID NO: 2; and
e) an isolated nucleic acid molecule degenerate from SEQ ID NO: 1 as a result of the genetic code.

The instant description states that the nucleic acid of SEQ ID NO: 1 encodes the amino acid of SEQ ID NO: 2, in the statement:

"SEQ ID NO: 1 representing the nucleotide sequence of RGL-alpha....SEQ ID NO: 2 representing the amino acid sequence of RGL-alpha." (page 11).
"The sequences of amino acids encoded by the DNA of SEQ ID Nos: 1 and 3 are shown as SEQ ID NO: 2 and 4, ***respectively***." (page 13).

Hence, the embodiment b) drawn to an isolated nucleic acid molecule encoding the amino acid sequence comprising SEQ ID NO: 2 would be the same in scope as that of e) which is a nucleic acid degenerate from SEQ ID NO: 1, the term, "degenerate," comprising the art-recognized meaning that the nucleic acid encodes the same protein.

Claim 1 is also indefinite because the phrase, "an isolated nucleic acid molecule degenerate from SEQ ID NO: 1 as a result of the genetic code," does not properly identify metes and bounds of the claim absent what the nucleic acid encodes as the term, "degeneracy" is defined as naturally occurring alternative codons which encode the ***same*** amino acid.

Claims 1, 2, and 6-8 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because the claims are not fully supported by the description. The application, as originally filed, did not describe:

Claims 1, 2, and 6-8 are drawn to the below embodiments:
a) SEQ ID NO: 1;

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

b) an isolated nucleic acid molecule encoding the amino acid sequence comprising SEQ ID NO: 2;
c) an isolated nucleic acid that hybridizes to either a) or b) under the recited moderate stringency;
d) an isolated nucleic acid molecule derived by *in vitro* mutagenesis from SEQ ID NO: 1; and
e) an isolated nucleic acid molecule degenerate from SEQ ID NO: 1 as a result of the genetic code.

It is determined that embodiments c) and d) do not meet written description requirement.

The nucleic acid of the embodiment of c) is not limited to a nucleic acid of any particular function so long as the nucleic acid hybridizes to SEQ ID NO: 1 or a nucleic acid encoding the protein of SEQ ID NO: 2. The instant description indicates that the invention is drawn to a nucleic acid and a polypeptide relating to RGL (RTVP-1-GliPR-like polypeptide, page 2, 2nd paragraph). The nucleic acid embraced by the embodiment c) is not limited to the nucleic acid of the invention but a genus embracing any nucleic acid that hybridizes to SEQ ID NO: 1 or a nucleic acid encoding the protein of SEQ ID NO: 2, the nucleic acid of which can have any functional characteristics. The instant description does not have a reasonable number of species embraced by the genus of the nucleic acid for embodiment c), and therefore, the claim lacks description.

The nucleic acid of the embodiment d) is also not limited to the nucleic acid of SEQ ID NO: 1 or the nucleic of SEQ ID NO: 2, but rather any nucleic acid comprising any mutation on any location of the nucleic acid of SEQ ID NO: 1. It is an art recognized practice that a nucleic acid of certain trait or phenotype can result from mutations. Since an isolated nucleic acid containing such mutation occurring in nature is in no way different from that which is produced by mutagenesis (product by process is a product claim absent structural difference produced by the process), and the instant description does not provide at least one species of nucleic acid comprising a mutation on SEQ ID NO: 1, or a reasonable number of species embraced by the genus, the claim lacks description.

Claim 2 drawn to a vector, claim 6 drawn to a host cell comprising the vector, claims 7-8 drawn to a method of using the nucleic acid, all depends from claim 1, which is not described. Therefore, the vector, the host cell, the method embracing nucleic acids which are not described cannot be described.

Claims 1, 2, and 6-8 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: Sine claims lack industrial applicability, a person skilled in the art would not know what to use the invention as claimed.